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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

IN RE APPLN. OF:	TAPER et al.	
SERIAL NO.:	09/700,573	
FILED:	November 16, 2000	
FOR:	SYNERGISTIC COMPOSITION FOR USE IN THE TREATMENT...	
GROUP:	1618	Confirmation No. 6030
EXAMINER:	ZOHREH, A. Fay	DOCKET: TEINSE RAFF.28

MAIL STOP APPEAL BRIEF - PATENTS
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

TRANSMITTAL LETTER

Dear Sir:

In response to the Examiner's Answer mailed November 17, 2005, enclosed please find the Appellants' Reply Brief. Appellants are also submitting a copy of the Claims on Appeal (Appendix A).

In the event there are any fee deficiencies or additional fees are payable, please charge them (or credit any overpayment) to our Deposit Account No. 08-1391.

Respectfully submitted,

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CERTIFICATE OF MAILING

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By M. Diane Dubé

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APPELLANTS' REPLY BRIEF UNDER 37 CFR 1.193 (b)

This Reply Brief is being filed in response to the new points of argument raised in the Examiner's Answer mailed November 17, 2005. Appellants respond to these new points of argument, as follows:

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STATUS OF CLAIMS ON APPEAL

Claims 21-33 and 35-42 remain pending in this application. Claims 21-33 and 35-42 stand finally rejected and are on appeal. The claims on appeal are set forth in Appendix A attached hereto.[1]

[1] Appendix A attached to Appellants' Main Brief on Appeal inadvertently failed to include claims 41 and 42. This is being corrected with the enclosed new Appendix A.

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

I. WHETHER THE REJECTION OF CLAIMS 35-40 UNDER 35 USC 112, FIRST PARAGRAPH, IS PROPER;[2] AND

II. WHETHER THE REJECTION OF CLAIMS 21-33 AND 35-42 UNDER 35 USC 102(b) AS BEING ANTICIPATED BY EUROPEAN PATENT APPLICATION O692252 IS PROPER.

[2] In the final rejection, Claims 21-33 and 35-42 were rejected under 35 USC 112, first paragraph. However, in her Answer, the Examiner limited the 112, first paragraph rejection to claims 35-40.

ARGUMENTS

I. THE REJECTION OF THE CLAIMS UNDER 35 USC §112, FIRST PARAGRAPH, IS IN ERROR.

As noted in footnote 1, *supra*, the Examiner appears to have limited her 112, first paragraph rejection to claims 35-40. Whether this was intentional, or whether the Examiner intended to include all of the claims on appeal, the fact remains the Examiner in rejecting the claims under 35 USC 112, first paragraph, has applied tests appropriate to new anti-cancer drugs, i.e., drugs, with heretofore unknown or unproven properties. As distinguished therefrom, the claims on appeal are all directed to a combination of a known anti-cancer drug, namely an anti-metabolic anti-cancer drug and a known nutritional supplement, inulin.

Contrary to the Examiner's position, Appellants' claims will not require undue experimentation. As the Examiner notes on page 4 of her Answer, the skill of the art is high, namely that of a Ph.D. or M.D. One skilled in the art certainly would have access to prior art information about the effects of anti-cancer drugs, in particular about (i) the various kinds of cancer that are preferably or most effectively treated with anti-metabolic anti-cancer drugs, and (ii) about which particular anti-metabolic anti-cancer drugs are most effective against given types of cancer (see Appendix D attached to Appellants' Main Brief on Appeal).

Besides, as a result of the definition, in fact the limitation, in the rejected claims of the kind of anti-cancer drug being an anti-metabolic anti-cancer drug, one skilled in the art inherently knows from the prior art against which kinds of cancer said anti-metabolic anti-cancer drugs are most effective and commonly used, and does not need to conduct undue experimentation to define the kinds of cancer against which the claimed combination is most effective and may be used.

Thus, one skilled in the art would not face an undue burden to find out by in-vitro empirical testing against which kinds of cancer a claimed combination of an anti-metabolic anti-cancer drug and inulin presents the most beneficial anti-cancer effects. Indeed, the subject invention does not read on compositions with qualitatively new anti-cancer effects, but on compositions that present, as a result of the synergistic effect discovered for the particular claimed combinations of the present invention, quantitatively enhanced anti-cancer effects.

Furthermore, because the claimed combination of an anti-metabolic anti-cancer drug and inulin does not relate to new anti-cancer effects, but rather to (synergistically) enhanced, known anti-cancer effects of known anti-cancer drugs, defining whether or not a claimed combination of an anti-metabolic anti-cancer drug and inulin presents enhanced anti-cancer effects (resulting from a synergistic effect) can be done by one of ordinary skill in the art by simple routine experimentation.

Moreover, unlike conventional combination chemotherapy, which, as the Examiner argues on the bottom of page 4 and the top of page 5 of her Answer, may be hit or miss propositions, the present claimed invention involves only a single anti-cancer drug, an anti-metabolic anti-cancer drug, and a nutritional supplement, inulin. Thus, cross-effects and interferences between active agents are not an issue with Appellants' claimed invention. And, unlike conventional screening for new anti-cancer drugs or even new combination chemotherapy which involves double-blind testing, with Appellants' claimed invention, a double-blind study would merely involve removing from a patient the inulin component. Thus, a patient participating in a double-blind study involving the instant claimed invention and receiving only the anti-metabolic anti-cancer drug component would be no worse off than had they not participated in the study, and simply took the same drug following conventional

treatment protocol. Compare this to double-blind studies of new anti-cancer drugs in which one patient may receive a potentially better drug, while the other patient receives the less desired drug or a placebo. In other words, simple in-vivo experiments are all that would be necessary to determine if taking the claimed combination of an anti-metabolic anti-cancer and inulin is better than taking the anti-metabolic anti-cancer drug by itself. While treatment protocols of human subjects with such combinations ultimately may require FDA approval, and consequently much more empirical clinical data, such data would not be necessary to enable one of ordinary skill in the art to practice the invention.

Furthermore, there is no unpredictability about the qualitative anti-cancer effects of the anti-metabolic anti-cancer drugs of the claimed combination. Admittedly, the quantitative anti-cancer effects (the level of the anti-cancer effects) of a particular combination of an anti-metabolic anti-cancer drug and inulin according to the present claimed invention may not be completely predictable, because the level of the effects may vary due to the particular combination used in the claimed composition, the particular kind of anti-metabolic anti-cancer drug and/or the degree of polymerisation of the inulin used, the stage of the cancer and the response of the individual patient to which the composition is administered, since variations in strength of effects are common for pharmaceutical compositions from patient to patient. However, these variations only relate to quantitative aspects of the anti-cancer effects of the claimed compositions, the determination thereof can easily be made simply by means of routine experiments. Consequently, there is no undue burden to determine the anti-cancer activities of a given particular combination of an anti-metabolic anti-cancer drug and inulin for use in the pharmaceutical composition according to the present claimed invention.

Accordingly, the rejection of the claims under 35 USC 112, first paragraph, is in error, and should be reversed.

II. THE REJECTION OF CLAIMS 21-33 AND 35-42 UNDER 35 USC 102(B) AS ANTICIPATED BY EP '252 LIKEWISE IS IN ERROR.

The prior art clearly teaches the use of inulin or oligofructose in combination with the claimed chemotherapeutic agents, such as methotrexate and flourorouracil for the treatment of cancer. This is not correct. Indeed, the particular combination of inulin or oligofructose with the claimed chemotherapeutic agents (anti-metabolic anti-cancer agents), such as methotrexate and flouorouracil, is not disclosed at all. EP 0692252 merely gives an enumeration of anti-cancer drugs (Listing from the Répertoire Commenté des Médicaments (1989)),[3] and selecting a combination comprising inulin and an anti-cancer drug from the large amount of possible combinations.

In rejecting the claims as anticipated by EP '252, the Examiner disregards certain language in the claims on appeal by ignoring the usual meaning of the word, and the meaning as used in Appellants' Specification in favor of her own definition for the term "synergistic." More particularly, the Examiner takes the word "synergistic" to mean merely "additive." However, as is clear from Appellants' Specification and the working examples contained therein, "synergistic" is employed by Appellants in its conventional manner, i.e., as meaning higher than the sum of the anti-cancer effects of the components taken separately. EP '252 nowhere teaches or suggests that the combination of an anti-metabolic anti-cancer drug and inulin would result in anti-cancer effects higher than the sum of the anti-cancer effects of the components taken separately.

[3]Appellants wish to correct a misstatement on page 8 of their Main Brief on appeal in which they stated: "Notably missing from this list [*] of useful classes of chemotherapeutic products is any mention of an anti-metabolic anti-cancer drug!" (Appellants' Main Brief, first sentence, on p. 8). [*]: List from the Répertoire Commenté des Médicaments (1989), given in Appellants' Brief, p. 7. Actually, two anti-metabolic anti-cancer agents are explicitly mentioned: methotrexate and fluorouracil. What Appellants meant to say is that there is no mention of a combination of anti-metabolic anti-cancer drugs and inulin.

At best, EP '252 teaches the additive effects of adding a chemotherapeutic agent by injection to an animal on a maintenance diet containing inulin/oligofructose. That is to say, EP '252 only details the efficacy of adding MNU, an alkylating agent, and doxorubicin. (EP '252 , Examples 1, 2, 3, and 7, pages 7-10). The administration of these agents is not concurrent and no observed effect of any kind is reported. In fact, it is believed that these agents would act solely in an additive manner. Indeed, this is consistent with Appellants' Specification, which reports on the concurrent administration of another alkylating agent (Endoxan instead of MNU) or doxorubicin with inulin/oligofructose acts only additively in their efficacy. (Specification at Table 1, page 14).

EP '252 mentions the possibility of compositions containing a combination of inulin and an anti-cancer drug. However, EP '252 merely contains a generic disclosure about a combination of inulin with an anti-cancer drug in general that has to be selected, without any teaching about the basis for said selection or about the manner to carry out said selection, from a long list of anti-cancer agents of various classes of anti-cancer drugs (EP '252, p. 3). EP '252 clearly thus not constitute an enabling disclosure.

Moreover, EP '252 is absolutely silent about a possible synergistic effect of any of those theoretically mentioned combinations of inulin and an anti-cancer drug. Example 7 of EP '252 can at most be considered as a merely speculative disclosure about synergistic effects. Example 7 describes one single experimental set up for identifying possible synergistic effects of a particular combination of an anti-cancer drug and an inulin, but no results of the experiment are disclosed, and thus certainly no results at all are disclosed about a possible synergistic effect of the combination of inulin and an anti-metabolic anti-cancer drug.

The particular combination explicitly disclosed by Example 7 of EP '252 merely relates to a combination of inulin (particularly oligofructose) and doxorubicine (an anti-mitotic anti-cancer drug) (see Specification, p. 2, line 22), not to the combination of inulin and an anti-metabolic anti-cancer drug. Accordingly, the Examiner's statements on page 6 of the Examiner's Answer that "The above reference [EP '252] makes clear that the claimed components [inulin or oligofructose and an anti-metabolic anti-cancer drug such as methotrexatre and fluorouracil] have been previously used in combination," is not at all correct.

Summarizing to this point, EP '252 is entirely silent as to a possible synergistic effect from a combination of inulin and an anti-metabolic anti-cancer drug. Thus, one skilled in the art reading EP '252 would interpret EP '252 as teaching that at best a combination of inulin and an anti-cancer drug may provide additive effects.

Appellants have found and demonstrated, through comparative test data (see Example, Table 1, page 14) that a synergistic effect present only in the case of an anti-metabolic anti-cancer drug when administered with inulin. That is to say, Table 1 in Appellants' Specification shows a synergistic anti-cancer effect only with a combination of inulin and an anti-metabolic anti-cancer drug, and no other anti-cancer drugs. Thus, and in the absence of prior art teaching in EP '252 of a synergistic effect of a combination of inulin and an anti-metabolic anti-cancer drug, Appellants' claims cannot be said to be anticipated by or for that matter obvious from EP '252.

Therefore, for the reasons discussed, *supra*, and in the Appellants' Main Brief, the rejection of claims 21-33 and 35-40 is in error.

CONCLUSION

In view of the foregoing, it is respectfully requested that the Examiner's Rejection of the subject Application be reversed in all respects.

Respectfully submitted,

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CERTIFICATE OF MAILING

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By M. Diane Dubé

NPS/ZD/dd

APPENDIX A TO
APPELLANTS' REPLY BRIEF

CLAIMS ON APPEAL

Serial No. 09/700,573
(Attorney Docket No. TIENSE RAFF .28)

APPENDIX A to APPELLANTS' REPLY BRIEF

CLAIMS ON APPEAL

21. Pharmaceutical composition characterized by comprising a combination of an effective dose of inulin and of an anti-metabolic anti-cancer drug, wherein said inulin and said anti-metabolic anti-cancer drug in combination provide a synergistic anti-cancer therapeutic effect to a human or non-ruminating animal undergoing treatment for cancer.

22. Pharmaceutical composition according to claim 21, wherein the inulin is inulin with a DP up to about 100, or oligofructose or a mixture thereof.

23. Pharmaceutical composition according to claim 21, wherein the inulin is chicory inulin with a ($\overline{DP}$) ranging from about 10 to about 30, or oligofructose with a (DP) ranging from 2 to 7 and containing about 5 wt% in total of glucose, fructose and sucrose.

24. Pharmaceutical composition according to claim 21, wherein the anti-cancer drug is selected from the group consisting of methotrexate, cytarabin, fluorouracil, mercaptopurin, thioguanin, azathioprin and hydroxycarbamide.

25. Pharmaceutical composition according to claim 24 wherein the anti-cancer drug is 5-fluorouracil or methotrexate.

26. Pharmaceutical composition according to claim 21, which additionally to the said anti-metabolic anti-cancer drug contains one or more anti-cancer drugs belonging to the class of anti-metabolic anti-cancer drugs and/or to another class of anti-cancer drugs.

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27. Pharmaceutical composition according to claim 21, in which the inulin and the anti-metabolic anti-cancer drug which constitute the combination are present in the same galenic formulation.

28. Pharmaceutical composition according to claim 21, in which the inulin and the anti-metabolic anti-cancer drug which constitute the combination are present in separate galenic formulations which in combination together form the pharmaceutical composition.

29. Pharmaceutical composition according to claim 21, which is suitable for oral, parenteral or rectal administration, or for tube feeding.

30. Pharmaceutical composition according to claim 28 in which the inulin is present in a functional food or feed.

31. Pharmaceutical composition according to claim 28 in which the anti-cancer drug is present in a formulation which is suitable for oral or parenteral administration.

32. Pharmaceutical composition according to claim 21 for use as a medicament for the treatment of cancer in human.

33. Pharmaceutical composition according to claim 21 for use as a medicament for the treatment of cancer in non-ruminating mammals.

35. Method for the treatment of cancer in a human or in a non-ruminating mammal comprising administering to said being in need of such treatment an effective amount of a pharmaceutical composition as defined in claim 21.

36. Method according to claim 35 wherein the inulin and the anti-metabolic anti-cancer drug of the combination forming the pharmaceutical composition are present in the same galenic formulation constituting the pharmaceutical composition.

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37. Method according to claim 35 wherein the inulin and the anti-metabolic anti-cancer drug of the combination forming the pharmaceutical composition are present in separate galenic formulations constituting together the pharmaceutical composition.

38. Method according to claim 37 wherein the separate galenic formulations are administered simultaneously or non-simultaneously.

39. Method according to claim 37 wherein the separate galenic formulations are administered via different methods of administration and the inulin is administered by a method selected from the group consisting of oral, parenteral or rectal administration and administration via tube feeding.

40. Method according to claim 39 wherein the separate galenic formulation containing the inulin is a functional food or feed.

41. Pharmaceutical composition according to claim 28, wherein the separate galenic formulations which in combination form the pharmaceutical composition are suitable for oral, parenteral or rectal administration, or for tube feeding.

42. Pharmaceutical composition according to claim 41, wherein the separate galenic formulations are suitable for administration in a different manner from each other.

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